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ORIGINAL INVESTIGATIONS

Long-Term Risk for Aortic Complications After Aortic Valve Replacement in Patients With Bicuspid Aortic Valve Versus Marfan Syndrome

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ABSTRACT

BACKGROUND Bicuspid aortic valves are associated with valve dysfunction, ascending aortic aneurysm and dissection. Management of the ascending aorta at the time of aortic valve replacement (AVR) in these patients is controversial and has been extrapolated from experience with Marfan syndrome, despite the absence of comparative long-term outcome data.

OBJECTIVES This study sought to assess whether the natural history of thoracic aortopathy after AVR in patients with bicuspid aortic valve disease is substantially different from that seen in patients with Marfan syndrome.

METHODS In this retrospective comparison, outcomes of 13,205 adults (2,079 with bicuspid aortic valves, 73 with Marfan syndrome, and 11,053 control patients with acquired aortic valve disease) who underwent primary AVR without replacement of the ascending aorta in New York State between 1995 and 2010 were compared. The median follow-up time was 6.6 years.

RESULTS The long-term incidence of thoracic aortic dissection was significantly higher in patients with Marfan syndrome (5.5 ± 2.7%) compared with those with bicuspid valves (0.55 ± 0.21%) and control group patients (0.41 ± 0.08%, $p < 0.001$). Thoracic aortic aneurysms were significantly more likely to be diagnosed in late follow-up in patients with Marfan syndrome (10.8 ± 4.4%) compared with those with bicuspid valves (4.8 ± 0.8%) and control group patients (1.4 ± 0.2%) ($p < 0.001$). Patients with Marfan syndrome were significantly more likely to undergo thoracic aortic surgery in late follow-up (10.4 ± 4.3%) compared with those with bicuspid valves (2.5 ± 0.6%) and control group patients (0.50 ± 0.09%) ($p < 0.001$).

CONCLUSIONS The much higher long-term rates of aortic complications after AVR observed in patients with Marfan syndrome compared with those with bicuspid aortic valves confirm that operative management of patients with bicuspid aortic valves should not be extrapolated from Marfan syndrome and support discrete treatment algorithms for these different clinical entities. (J Am Coll Cardiol 2015;65:2363–9) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AVR = aortic valve replacement

CI = confidence interval

HR = hazard ratio

ICD-9-CM = International Classification of Diseases-Ninth Revision-Clinical Modification

TAA = thoracic aortic aneurysm

The prevalence of bicuspid aortic valves in the general population is approximately 1% (1). Bicuspid valves degenerate more frequently and rapidly than trileaflet aortic valves, and recent clinical history data suggest that as many as 50% of patients with echocardiographic diagnoses of bicuspid aortic valve eventually require aortic valve replacement (AVR) (2,3). The incidence of ascending aortic dissection in patients with bicuspid aortic valves is estimated to be 8 times higher than that in the general population (2), but single-center studies focusing on the long-term risk for dissection after isolated AVR in patients with bicuspid aortic valves have yielded conflicting outcome data (4–8), so the indications for concomitant intervention on the thoracic aorta at the time of AVR are controversial (9). Histopathologic similarities between specimens of aneurysms from patients with bicuspid aortic valves and Marfan syndrome (10,11) have led to the extrapolation of treatment algorithms for management of the ascending aorta in bicuspid aortic valve disease from aggressive guidelines established for the management of Marfan syndrome (12,13), despite the lack of supporting comparative clinical outcome data (14,15). This study was designed to test the hypothesis that the natural history of thoracic aortopathy after AVR in patients with bicuspid aortic valve disease is substantially different from that seen in patients with Marfan syndrome.

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METHODS

STUDY DESIGN. In this retrospective comparison, long-term outcomes of adult patients with bicuspid aortic valves, those with Marfan syndrome, and a control group of patients with acquired aortic valve disease undergoing primary AVR without concomitant thoracic aortic surgery in New York State between January 1, 1995, and December 31, 2010, were compared according to the etiology of aortic valve disease. Patients were identified using the Statewide Planning and Research Cooperative System, an all-payer, administrative database that prospectively collects data on every hospital discharge, ambulatory surgery, and emergency department visit in New York State. Patients undergoing AVR were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes 35.21 and 35.22. Patients with bicuspid valves were identified using ICD-9-CM code 746.4. The prevalence of bicuspid aortic valves in this cohort was 3.9%, suggesting that it is underdiagnosed in comparison with clinical registries of patients undergoing AVR (16,17). Therefore, to more accurately identify a control group that did not contain a substantial number of patients with undiagnosed bicuspid valve, we selected patients undergoing AVR with diagnoses of chronic rheumatic aortic valve disease (ICD-9-CM codes 395.0, 395.1, 395.2, 395.9, 396.0, 396.1, 396.2, 396.3, 396.8, and 396.9). Patients with Marfan syndrome were identified using ICD-9-CM code 759.82, from any hospital admission before or after surgery.

Exclusion criteria were age < 18 years; out-of-state residence; any history of thoracic aortic aneurysm (TAA), thoracic aortic dissection, or thoracic aortic rupture; concomitant thoracic aortic surgery; prior thoracic aortic surgery; prior coronary artery bypass grafting; and prior replacement or repair of any valve (Online Table 1). Patients with the following genetic syndromes and inflammatory diseases associated with TAA and dissection also were excluded: Turner syndrome, Ehlers-Danlos syndrome, Shone complex, Takayasu arteritis, giant cell arteritis, Behçet disease, and ankylosing spondylitis (Online Table 1). Patients undergoing concomitant coronary artery bypass grafting and other valve surgery were not excluded.

Baseline comorbidities were identified using diagnosis codes from the index hospitalization and all hospitalizations up to 2 years before the index hospitalization (Online Table 2). The Data Protection Review Board of the New York State Department of Health, as well as the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai, approved the study. The approval included a waiver of informed consent.

STUDY ENDPOINTS. The primary outcome measure was the cumulative incidence of thoracic aortic dissection (441.01 and 441.03) or rupture (441.1 and 441.6). Abdominal aortic dissection (441.02) or rupture (441.3) was not included. Secondary outcome measures included the cumulative incidence of TAA (441.2 and 441.7) and thoracic aortic surgery (38.34 and 38.45), as well as overall survival. Deaths were identified using the Social Security Death Master File (current as of November 30, 2013) and by searching all hospital admissions, ambulatory, or emergency department visits for patient deaths. Patients for whom no thoracic aortic dissection or rupture, TAA, or thoracic aortic surgery was found were censored on December 31, 2012 (the last date of follow-up by the Statewide Planning and Research Cooperative System).